Original Article

Efficacy of Tramadol in Preventing the Post-Anesthetic Shivering After General Anesthesia for Cholecystectomy

Ali Ammar, Muhammad Ali Mahota, M. Asif and Aamir Furqan

ABSTRACT

Objective: To study the efficacy of tramadol in preventing the post-anesthetic shivering after general anesthesia for laparoscopic or open cholecystectomy.

Study Design: A randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of Anaesthesia Nishtar Hospital Multan, From September 5, 2017 to December 15, 2017.

Materials and Methods: A sample of thirty six patients was taken using non-probability consecutive sampling technique. Age, weight, baseline heart rate and mean arterial pressure; temperature before and after surgery and their difference; and degree of shivering and sedation in recovery period were recorded. Chi-square test and one way ANOVA test were applied to compare percentages/nominal data and means, respectively using SPSS v.23 and $p \leq 0.05$ was considered statistically significant.

Results: Considering the treatment groups, the postoperative shivering was 88.9% and 11.1% in group-L1; and 77.7% and 22.2% in group-O1, of grade 0 and 1, respectively. Both the groups were comparable and shivering of grade 2, 3 or 4 was not seen in both these groups. Considering the control groups, postoperative shivering was 22.2% grade 0, 55.5% grade 1, 11.1% grade 2, and 11.1% grade-3 in Group-L2; and 33.3% grade-0, 44.45 grade 1, and 22.2% grade 2 in group-O2. The difference between treatment and control group was statistically significant ($p=0.005$).

Conclusion: Our study concludes that tramadol, when given in adequate doses, is effective in preventing postoperative shivering after laparoscopic and open cholecystectomy.

Key Words: Post-anesthetic shivering, Core temperature, Tramadol, Laparoscopic Cholecystectomy, Open cholecystectomy

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INTRODUCTION

When patients are recovering from general anesthesia, their most common experience is shivering. Almost 60% of the patients go through this experience. The control of autonomic thermoregulatory system is compromised whenever a patient undergoes a general anesthesia[1]. Four basic mechanisms of heat transmission [2, 3] i.e. Conduction, convection, radiation and evaporation are responsible for the loss of heat from skin. Radiation is the most prominent culprit in this scenario. Radiation is the phenomenon in which heat is transferred from one surface, via photons, to another one and is not affected by the temperature of the interfering air. Conduction is the transfer of heat directly from one surface to another adjacent one and is directly proportional to the difference in the temperature of the two surfaces. The transfer of heat by the movement of fluids in between two surfaces is called convection. The drop in body temperature is augmented by cold intravenous infusions, dry and cold gases used in anesthesia [4], absent muscular activity, sub dermal vasodilation and cold atmosphere of the operation theatre [5]. All of these factors contribute to hypothermia which is thought to be the primary cause of post-anesthetic shivering.

It is well-known that core hypothermia is more marked in large operations as compared to small operations; and it is contributed mostly by the loss of heat via evaporation. A fall of 1 ^{o}C in core body temperature results in shivering [6]. Shivering is defined as a spontaneous, oscillatory muscle movement that enhances metabolic heat generation. It can be a very spiteful experience for the patients who are recovering from general anesthesia. Many patients describe this feeling to be worse than the post-surgical pain. Shivering is physiologically hectic and results in more oxygen depletion [7], rise in intraocular as well as intracranial pressure, lactic acidosis, arterial hypoxemia, and over activity of sympathetic nervous system. Many pharmacologic agents have been tried in an attempt to prevent this unpleasant outcome, keeping

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above mentioned effects in view, but the exact basis is not understood so far [8].

According to some studies, the use of tramadol resulted in total elimination of post-anesthetic shivering. Tramadol is a synthetic opioid. It is thought to inhibit shivering by blocking the reuptake of serotonin, dopamine and norepinephrine [9]. Activity of the nucleus median raphe in the medulla is also controlled by tramadol, via its effect on central m opioid receptor, primarily. Its effect over k-receptors is least. The most reported side effects of tramadol are nausea, vomiting, constipation, lightheadedness, dizziness, drowsiness, or headache. When the patient is taking other drugs that enhance serotonin level, the chances of serotonin syndrome increase[10]. The risk of toxicity and severe side effects (dizziness, drowsiness and shallow breathing) also increases when other opioids for example pain relievers (codeine) and cough relievers (hydrocodone) are being used. Therefore, tramadol needs to be used carefully in such patients.

The current study is aimed at determining the efficacy of tramadol in reducing or avoiding the shivering that occurs after the general anesthesia, when it was administered in adequate doses before closing the wound, in the patients undergoing cholecystectomy, either through laparoscopic or open surgery.

MATERIALS AND METHODS

This study is a randomized controlled trial. The study was performed in Department of Anaesthesia Nishtar Hospital, Multan, after taking consent from the department ethical committee, over a period from 5 September 2017 to 15 December 2017. The study by Angral R. et al. [11] was taken as reference and non-probability consecutive sampling technique was used to select the sample size. Total of thirty six patients who were planned to undergo cholecystectomy, either via laparoscopic (Group-L) or open procedure (Group-O), were included in our study. Both the groups were further divided indiscriminately into two groups, having nine patients each (Group L1, L2, O1 and O2); the treatment groups which were to receive 1mg/kg body weight of tramadol (Group L1 and O1) and the control groups which were to receive a corresponding dose of normal saline (group L2 and O2), before closure of the wound during surgery.

Patients were thoroughly examined and investigated. After reaching the operation theatre, baseline heart rate and mean arterial pressure were recorded after attaching the monitor. Patients were pre-oxygenated with 100% oxygen. Anesthesia was induced using intravenous propofol, followed by vecuronium bromide 0.1mg/kg injection. Endotracheal tube was inserted and fixed. Nasopharyngeal temperature probe was inserted because it lies closest to the base of brain and baseline temperature was recorded. The reading was highly precise and was not affected by breathing or turning of head. Operating room temperature was maintained at 22-24 ^{o}C. Patients were covered with sterilized sheets but were not warmed actively. Diclofenac Sodium was used for analgesia during operation, as an intravenous infusion of 1.5mg/kg body weight diluted in 100ml of normal saline. Required changes were made to maintain oxygen saturation at 98-100%, following pneumoperitonium in the patients undergoing laparoscopic surgery. Tramadol 1mg/kg body weight or equivalent dose of normal saline was given intravenously to the corresponding groups, just before closing the wound during surgery. Nasopharyngeal temperature was recorded again at the end of surgery. Proper doses of neostigmine and glycopyrrolate were used to reverse the neuromuscular blockade. In the recovery room, all the patients were covered with wool blankets and 28% oxygen was given with vent mask.

An observer, who had no knowledge of the nature of the surgical procedure, recorded pulse rate, mean arterial pressure, degree of sedation and grade of post anesthetic shivering after every five minutes, for half an hour. The criteria presented by Crossley and Mahajan [12] was used to assess the grade of post anesthetic shivering. (Table-1). Table-2 as used to assess the grade of sedation. Tramadol 1mg/kg was given to control the shivering. The patients who had suffered from some severe febrile illness, had respiratory illness which could compromise breathing and received sedatives or narcotics in recent preoperative period, were excluded from our study. Age, weight, baseline heart rate and mean arterial pressure; temperature before and after surgery and their difference; and degree of shivering and sedation in recovery period were recorded on a preformed Performa, by the researcher himself. Chi-square test and ANOVA test were applied to compare percentages/nominal data and means, respectively. Data was analyzed using SPSS v.23 and value of $p \leq 0.05$ was considered statistically significant.

RESULTS

Mean age, mean weight were 35.78±3.9 years and 56.1±5.47 Kg in group-L1; 37±4.87 years and 56.02±2.74 kg in group-L2; 36.67±3.6 years and 55.04±5.47 Kg in group-O1; and 34.56±4.95 years and 53.78±6.83 Kg in group-O2, respectively. The male to female ratio was 7:2 in all the groups. (Table-3)

The baseline heart rate and mean arterial pressure was 90.56±3.64/min and 92.00±2.74 mmHg in group-L1; 89.22±4.82/min and 90.67±3.39 mmHg in group-L2; 88.56±3.50/min and 92.33±3.39 mmHg in group-O1; and 90.78±3.93/min and 91.11±2.57 mmHg in group-O2, respectively. The differences were not statistically significant ($p>0.05$). Duration of surgery and anesthesia was 115.67±11.64min and 122.33±10.51min in group-L1; 117.67±10.35min and 123.88±10.28min in group-L2; 95.00±15.61min and 101.44±14.65min in group-O1; and 96.67±16.39min and 102.44±16.88min in

group-O2, respectively. The differences were statistically significant (p<0.05). (Table-4). Mean preoperative temperature, postoperative temperature and the difference in temperature was 36.6±0.27ºC, 36.03 ±0.43ºC and 0.56±0.42ºC in group-L1; 36.48±0.29ºC, 36.10±0.35ºC and 0.38±0.21ºC in group-L2; 36.47±0.39ºC, 36.28±0.48ºC and 0.18±0.14ºC in group-O1; and 36.63±0.36ºC, 36.42±0.41ºC and 0.21±0.10ºC in group-O2, respectively. There was a significant drop in temperature in patients undergoing laparoscopic and open cholecystectomy (p=0.009). (Table-5)

Considering the treatment groups, the postoperative shivering was 88.9% and 11.1% in group-L1; and 77.7% and 22.2% in group-O1, of grade 0 and 1, respectively. Both the groups were comparable and shivering of grade 2, 3 or 4 was not seen in both these groups. Considering the control groups, postoperative shivering was 22.2% grade 0, 55.5% grade 1, 11.1% grade 2, and 11.1% grade-3 in Group-L2; and 33.3% grade-0, 44.45 grade 1, and 22.2% grade 2 in group-O2. The differences were statistically significant (p=0.005). (Table-6) Postoperative sedation of grade 0 and 1 was 77.7% and 22.2% in group-L1; 66.6% and 33.3% in group-L2; 66.6% and 33.3% in group-O1; and 77.7% and 22.2% in group-O2, respectively. All the groups were comparable and postoperative sedation of grade 2, 3 or 4 was not seen in any of these groups. (Table-7).

Table No.1: Grade of Shivering

Grade	Clinical Signs
0	No Shivering
1	peripheral vasoconstriction or Piloerection, but shivering not visible
2	Muscular activity (fasciculation) in only one muscle group
3	Muscular activity in more than one muscle group, but no generalized shivering
4	Shivering involving the whole body, with generalized shaking

Table No.2: Grades of Sedation

Grade	Clinical Signs
0	Alert
1	Arouse to voice
2	Arouse with gentle tactile stimulus
3	Arouse with vigorous tactile stimulus
4	No awareness

Table No.3: Demographic Details

Varia-ble	Group-L1	Group-L2	Group-O1	Group-O2
Age (years)	35.78±3.9	37±4.87	36.67±3.6	34.56±4.95
Weight (Kg)	56.1±5.47	56.02±2.74	55.04±5.47	53.78±6.83
Male/Female Ratio	7:2	7:2	7:2	7:2

Values are Mean ± S.D or Ratio

Table No.4: Baseline Vitals and Surgery duration

Variable	Group-L1	Group-L2	Group-O1	Group-O2
Heart Rate (beats/min)	90.56±3.64	89.22±4.82	88.56±3.50	90.78±3.93
MAP (mmHg)	92.00±2.74	90.67±3.39	92.33±3.39	91.11±2.57
Surgery Duration (min)*	115.67±11.64	117.67±10.35	95.00±15.61	96.67±16.39
Anesthesia Duration (min)*	122.33±10.51	123.88±10.28	101.44±14.65	102.44±16.88

Values are Mean ± S.D or Number; MAP=mean arterial pressure; *p>0.05 and is significant.

Table No.5: Variation in Temperature (ºC)

Variable	Group-L1	Group-L2	Group-O1	Group-O2
Preoper a-tive	36.60±0.27	36.48±0.29	36.47±0.39	36.63±0.36
Postoper a-tive	36.03 ±0.43	36.10±0.35	36.28±0.48	36.42±0.41
Differ-ence*	0.56±0.42	0.38±0.21	0.18±0.14	0.21±0.10

Values are Mean ± S.D or Number; *p=0.009, statistically significant fall in temperature

Table No.6: Incidence of Post-Operative Shivering According To Severity

Grade	Group-L1	Group-L2	Group-O1	Group-O2
0	8(88.9)	2(22.2)	7(77.7)	3(33.3)
1	1(11.1)	5(55.5)	2(22.2)	4(44.4)
2	0	1(11.1)	0	2(22.2)
3	0	1(11.1)	0	0
4	0	0	0	0

Values are numbers and percentages, N (%); p=0.005, statistically significant.

Table No.7: Incidence of Post-Operative Sedation According To Severity

Grade	Group-L1	Group-L2	Group-O1	Group-O2
0	7(77.7)	6(66.6)	6(66.6)	7(77.7)
1	2(22.2)	3(33.3)	3(33.3)	2(22.2)
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0

Values are numbers and percentages, N (%); p>0.05, not significant.

DISCUSSION

In our study, we deduced that tramadol at a dose of 1mg/kg caused a significant decrease in post anesthetic shivering in patients undergoing cholecystectomy, regardless of laparoscopic or open surgical procedure. These effects were noted when the patients were in recovery room and were under no or mild sedation.

Angral R. et al. [11] concluded in their study that tramadol was safe and effective for prevention of postoperative shivering after open and laparoscopic cholecystectomy, when given in a dose of 1 mg/kg. They observed minimum side effects at this dose level. In a study, conducted by Heidari SM et al.[13] in 2014, they revealed that the incidence of high grade post anesthetic shivering was considerably lower in the group receiving tramadol at the end of surgery as compared to the group which received placebo. But the overall prevalence of post anesthetic shivering was not different in both groups. They suggested that increasing the dosage of tramadol can have better effects on reducing shivering. Both of these studies produced results that are in agreement with the results of our study.

In a recent study, Nakagawa T. et al.[14], while studying the effects of tramadol on post anesthetic shivering after general anesthesia with remifentanil and sevoflurane, established that post anesthetic shivering was significantly reduced after administration of tramadol. This response of tramadol was independent of the concentration of remifentanil at the time of induction of anesthesia. According to them, tramadol can be a suitable drug for the prevention of post anesthetic shivering. A randomized control trial by Yousuf B.[15] produced the similar results. This study concluded that the need for treatment of post anesthetic shivering and pain was reduced when a 1mg/kg prophylactic dose of tramadol was given to the patients.

Tewari A. et al. [16] compared the effects of tramadol and clonidine over post anesthetic shivering in elderly patients undergoing transurethral resection of prostate under subarachnoid block. They came to conclusion that tramadol was comparable to clonidine in reducing the severity and duration of post anesthetic shivering but tramadol has a plus point of decreasing postoperative pain. Mahesh T. et al [17] compared the post anesthetic effects of tramadol and pethidine which showed tramadol to be better agent with respect to producing earlier and enhanced anti-shivering effects. Dhimar AA [18] also compare tramadol with pethidine and found tramadol to be qualitatively better in terms of being more potent in controlling the post anesthetic shivering and its relapse.

In contrast with our results, Shukla U. [19] found out that tramadol took longer time to attain full cessation of post anesthetic shivering in the patient who were given spinal anesthesia. The incidence of side effects was also frequent with tramadol.

There is need to conduct further studies to compare the effects of tramadol on post anesthetic shivering with different types of anesthesia.

CONCLUSION

Our study concludes that tramadol, when given in adequate doses, is effective in preventing postoperative shivering in patients undergoing laparoscopic and open cholecystectomy, when compared with patients who were injected intravenously with equivalent doses of normal saline.

Author's Contribution:

Concept & Design of Study:	Ali Ammar
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REFERENCES

1. Sessler DI. Perioperative thermoregulation and heat balance. Lancet 2016;387(10038):2655-64.
2. Lienhard JH. A heat transfer textbook. Courier Corporation; 2013.
3. Serth RW, Lestina T. Process heat transfer: Principles, applications and rules of thumb. Academic Press; 2014.
4. Oshvandi K, Shiri FH, Fazel MR, Safari M, Ravari A. The effect of pre-warmed intravenous fluids on prevention of intraoperative hypothermia in cesarean section. Iran J Nurs Midwifery Res 2014;19(1):64.
5. Cannistraro G, Cannistraro M. Hypothermia risk, monitoring and environment control in operating rooms. Int J Heat Tech 2016;34(2):165.
6. Rajagopalan S, Mascha E, Na J, Sessler DI. The effects of mild perioperative hypothermia on blood loss and transfusion requirement. Anesthesiol 2008;108(1):71-7.
7. Gecaj-Gashi A, Hashimi M, Sada F, Salihu S, Terziqi H. Prophylactic ketamine reduces incidence of postanaesthetic shivering. Niger J Med 2010;19(3):267-70.
8. Mahamood MA, Zweifler RM. Progress in shivering control. J Neurol Sci 2007;261:47–54.
9. Vazzana M, Andreani T, et al. Tramadol hydrochloride: pharmacokinetics, pharmaco-dynamics, adverse side effects, co-administration of drugs and new drug delivery systems. Biomed Pharmacother 2015;70:234-8.
10. Kaye AD. Tramadol, pharmacology, side effects, and serotonin syndrome: a review. Pain physician 2015;18:395-400.

11. Angral R, Wani AA, Kapoor BB. Tramadol and postoperative shivering in patients undergoing open and laparoscopic cholecystectomy under general anaesthesia. S Afr J Anaesth Analg 2012;18(2).
12. Crossley AW, Mahajan RP. The intensity of postoperative shivering is unrelated to axillary temperature. Anaesthesia 1994;49(3):205-7.
13. Heidari SM, Rahimi M, Soltani H, Hashemi SJ, Shabahang S. Premedication with oral tramadol reduces severity of postoperative shivering after general anesthesia. Adv Biomed Res 2014;3.
14. Nakagawa T, Hashimoto M, Hashimoto Y, Shirozu K, Hoka S. The effects of tramadol on postoperative shivering after sevoflurane and remifentanil anesthesia. BMC Anesthesiol 2017; 17(1):1.
15. Yousuf B, Samad K, Ullah H, Hoda MQ. Efficacy of tramadol in preventing postoperative shivering using thiopentone or propofol as induction agent: A randomized controlled trial. J Anaesthesiol Clin Pharmacol 2013;29(4):521.
16. Tewari A, Dhawan I, et al. A comparative study evaluating the prophylactic efficacy of oral clonidine and tramadol for perioperative shivering in geriatric patients undergoing transurethral resection of prostate. J Anaesthesiol Clin Pharmacol 2014;30(3):340.
17. Mahesh T, Kaparti L. A randomised trial comparing efficacy, onset and duration of action of pethidine and tramadol in abolition of shivering in the intra operative period. J Clin Diagn Res 2014;8(11):GC07.
18. Dhimar AA, Patel MG, Swadia VN. Tramadol for control of shivering (comparison with pethidine). Indian J Anaesth 2007;51(1):28.
19. Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. Indian J Anaesth 2011;55(3):242.